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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/562,010

12/23/2005

Akito Yasuhara

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EXAMINER

LAO, MARIALOUISA

ART UNIT

PAPER NUMBER

1621

MAIL DATE

DELIVERY MODE

08/03/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

Application No.

10/562,010

Applicant(s)

YASUHARA ET AL.

Examiner

M. Louisa Lao

Art Unit

1621

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 9-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 22-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 12/23/2005.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_.

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## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election without traverse of Group II:  $R^1$  and  $R^2 = H$ ,  $X=f$ ,  $Y = -S(O)_nR^7$  where  $n=1$  and  $R^7$  = phenyl group in the reply filed on 6/7/07 is acknowledged.
2. Claims 9-21 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/7/07.

The requirement is still deemed proper and is therefore made FINAL.

### *Claim Rejections - 35 USC § 103*

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

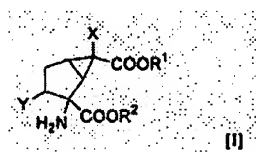
5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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6. **Claims 1-8 and 22-25 are rejected** under 35 U.S.C. 103(a) as being unpatentable over Fernandez et al. (US5912248, US'248).

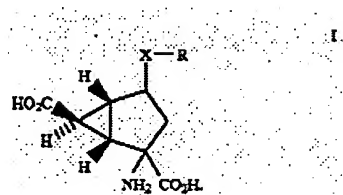
*Applicant Claims*

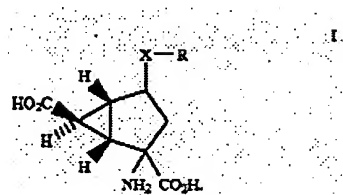
7. The instant claims are drawn to an 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by



formula [I], where the substituents are therein defined; and a drug comprising said derivative, the pharmaceutically acceptable salt thereof or the hydrate thereof as a Group II metabotropic glutamate receptor antagonist.

*Determination of the Scope and Content of the Prior Art  
(MPEP §2141.01)*



7. US' 248 teaches the compounds of the formula , where X represents a bond, S, SO, or SO<sub>2</sub>; and R is, *inter alia*, (1-6 C) alkyl group, a (2-6C) alkenyl group; a (2-6C) alkynyl group; an optionally substituted aromatic group, etc. In columns 9-10, US'248 teaches that the compounds of said formula are formulated into a pharmaceutical formulation and with experiments have demonstrated the ability to affect excitatory amino acid receptors and their affinity for metabotropic glutamate receptors, as both antagonists or agonists.

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***Ascertainment of the Difference  
Between Scope of the Prior Art and the Claims  
(MPEP §2141.012)***

8. US'248 differs from instant claims by the position of the Y-substituent in the latter (the X-R substituent in the former).

***Finding of Prima Facie Obviousness Rational and Motivation  
(MPEP §2142-2143)***

9. At the time of the invention, one of ordinary skill in the art looking to develop compounds that have affinity for metabotropic glutamate receptors would have found it *prima facie* obvious to start with the teachings of the cited prior art reference. It would have been obvious to modify the cited prior art compound of formula I, since it is within the purview of artisan through routine experimentation, to look for and develop similar compounds that exhibit a known utility without an inordinate degree of experimentation with a reasonable expectation of success.

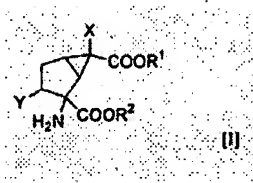
10. Thus, claims 1-8 and 22-25 are obvious over the cited prior art reference.

11. **Group II:**  $R^1$  and  $R^2 = H$ ,  $X=f$ ,  $Y = -S(O)_nR^7$  where  $n=1$  and  $R^7 =$  phenyl group is rejected under 35 U.S.C. 103(a) as being unpatentable over Fernandez et al. (US5912248, US'248) in view of Silverman. The Organic Chemistry of Drug Design and Drug Action. Academic Press:1992, pp15-22.

***Applicant Claims***

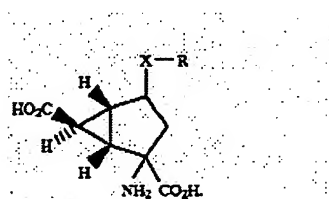
7. The instant claims are drawn to an 2-amino-bicyclo [3.1.0] hexane-2,6-dicarboxylic acid derivative, a pharmaceutically acceptable salt thereof or a hydrate thereof, represented by

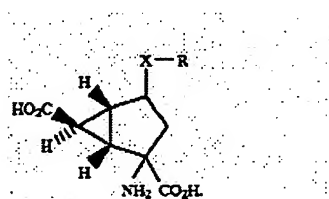
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formula [I], where the substituents are therein defined; and a drug comprising said derivative, the pharmaceutically acceptable salt thereof or the hydrate thereof as a Group II metabotropic glutamate receptor antagonist.

***Determination of the Scope and Content of the Prior Art  
(MPEP §2141.01)***



12. US' 248 teaches the compounds of the formula , where X represents a bond, S, SO, or SO<sub>2</sub>; and R is, *inter alia*, (1-6 C) alkyl group, a (2-6C) alkenyl group; a (2-6C) alkynyl group; an optionally substituted aromatic group, etc. In columns 9-10, US'248 teaches that the compounds of said formula are formulated into a pharmaceutical formulation and with experiments have demonstrated the ability to affect excitatory amino acid receptors and their affinity for metabotropic glutamate receptors, as both antagonists or agonists.

***Ascertainment of the Difference  
Between Scope of the Prior Art and the Claims  
(MPEP §2141.012)***

13. US'248 differs from instant claims by the position of the Y-substituent in the latter (the X-R substituent in the former) and X-substituent in the latter as either H or F (the former has H).

***Finding of Prima Facie Obviousness Rational and Motivation  
(MPEP §2142-2143)***

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14. At the time of the invention, one of ordinary skill in the art looking to develop compounds that have affinity for metabotropic glutamate receptors would have found it *prima facie* obvious to start with the teachings of the cited prior art references. It would have been obvious to modify the compound of formula I in US`248 since Silverman is relied upon to show in pages 19-22 that bioisosteres are substituents or groups that have chemical or physical similarities, and which produce broadly similar biological properties. As illustrated by the substitution of H for F; or, similarly, for the positional isomer for the X-R of US`248 for the instant Y-substituent. It would have been obvious to adapt these modifications, since the artisan at the time of the invention is compelled by routine experimentation, to look for and develop similar compounds that exhibit a known utility without an inordinate degree of experimentation with a reasonable expectation of success.


15. Thus, the teachings of the cited prior art references are fairly suggestive of the *prima facie* obviousness of Group II.

16. No claims are allowed.

### *Correspondence*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MLouisa Lao whose telephone number is 571-272-9930. The examiner can normally be reached on Mondays to Thursdays from 8:00am to 8:00pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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MLouisa Lao  
Examiner  
Art Unit 1621

  
for YVONNE EYLER  
SUPERVISORY PATENT EXAMINER  
TC1600 GAU 1621